UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/284,147	03/17/99	LANQUETIN M	GEI-067

HM22/0531

BIERMAN MUSERLIAN AND LUCAS
600 THIRD AVENUE
NEW YORK NY 10016

EXAMINER	
QAZI,S	
ART UNIT	**PAPER NUMBER**
1616	10

DATE MAILED: 05/31/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
09/284,147	Lanquetin et al.
Examiner	**Group Art Unit**
Sabiha Qazi	1616

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☐ expires _____ months from the mailing date of the final rejection.

b) ☒ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on _____ (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on *May 8, 2000* **has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:**

☐ The proposed amendment(s):

☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☐ Applicant's response has overcome the following rejection(s):

_____

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
Amended claims are not allowable. Prior art teaches the instant invention. Amendments are entered.

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: *None*

Claims objected to: *None*

Claims rejected: *22-34*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☒ Other *Please see attachment to advisory.*

Attachment to Advisory Action

Status of the Application

Claim 21 is canceled.

New claim 34 is added.

Claims 22-34 are pending.

Claims 22-34 are rejected.

Applicant's response in paper no. 9, dated 5/8/00 is hereby acknowledged. Amendments are entered.

Rejection Withdrawn

Claims 21-33 are rejected under 35 U.S.C. 103(a) as obvious over Conard et al. (Fertility and sterility, vol. 64 (4), (1995), pages 957-962) and Cano et al. (CA 115:150824, abstract of Maturitas (1991), 13(1), 35-42) are withdrawn because claims are amended. Rejections under 112 (1) is withdrawn because applicants arguments are found persuasive.

An English translation of Sitruk-Ware (Accession number 96148040, MEDLINE, abstract of Rev. Prat, (1995), 45(19) pages 2401-2406) is enclosed with this office action.

Rejection Maintained

Fraser et al. (Medline, AN 89261206, abstract of Maturitas, (1989 Mar) 11(1), 21-34) and Lanquetin et al. (US Patent

5,891,867) are maintained for the same reasons set forth in office action mailed in paper no. 6, dated 9/23/99. New claim 34 falls under the same scope therefore is rejected on the same basis.

Response to Arguments

Applicant's arguments filed on 5/8/00 are considered but are not found persuasive. Following reasons apply:

1. The basis of the arguments is that amended claims are allowable and prior art does not tech the instant invention.Even though claims are amended the invention is obvious over the prior art.

The amended claims now are drawn to the methods of treating hypoestrogenism in women and avoiding the appearance of withdrawal bleeding in post-menopausal comprising orally administering from 21- 25 days simultaneously, an estrogenic compound and a progestogenic compound consisting of nomegesterol acetate.

2. Examiner respectfully disagree with the arguments because the prior art teaches the instant invention. See Fraser references, lines 15 and 16 of abstract, where all patients

experienced a regular, progestrogen-induced withdrawal bleed each month. Nomegestrol acetate as a potent progestrogen are taught.

3. Applicant is requested to see US '587, lines 28-59, col. 2, where the delay in the occurrence of bleeding after the treatment was stopped. The 17β-estradiol units for 10 days (D1 to day D10 days). The units of combination of 17β-estradiol and nomegesterol acetate for fourteen consecutive days (day D11 to day D25). The placebo units for six days (day D25 to day D30). See lines 25-62, col. 1). The amount of the active principle ranging from 1-3 mg of b estradiol, combination of estradiol and nomegestrol acetate ranging from 1-3 mg and 1.5 to 6 mg.

4. Examiner respectfully disagree because the estradiol/progestrone combination is taught by the prior art for the same use as is instantly claimed. The treatment by the same combination for extended days would have been obvious to one who is familiar with the art. Note, that the total days of treatment by the prior art is 24 days, 14 consecutive using combination and 10 using estradiol alone.

It would have been obvious to one who is familiar with the art to extend the dosage to further avoid the appearance of bleeding in post-menopausal woman.

The data showing any unexpected results would overcome the above 35 U.S.C. 103(a) rejection.

Since the invention is obvious over the prior art, applicant is requested to file a side by side comparison in the form of a declaration for any unexpected results. See MPEP 716.02(e). The declaration must show that extended dosage as claimed was unexpected.

Basis of rejection

1. Claims 22-34 are rejected under 35 U.S.C. 103(a) as obvious over Fraser et al. (Medline, AN 89261206, abstract of Maturitas, (1989 Mar) 11(1), 21-34).

Fraser teaches the effects of the addition of nomegestrol acetate to post menopausal teach addition of progestogen to the oestrogen in order to prevent endometrial abnormalities. See the abstracts.

The instant claims differ from the reference in having different generic scope. The instant invention is broader than the prior art by claiming the simultaneous administration of

estrogenic and progestative compounds for estrogenic deficiencies.

One having ordinary skill in the art would have been motivated to prepare additional beneficial composition and method for the treatment of estrogenic deficiencies,

estradiol/progestrone for the treatment of post menopause estrogen deficiencies by using the combination with a estrogen and a compound with progestational activity because prior art teaches that estradiol in combination with a progestative compound for the treatment of estrogenic deficiencies.

There has been ample motivation provided by the prior art to prepare such combination when searching for the compositions of the similar activity.

Claim 26 is drawn to estradiol valerate are known esters and property associated with the estradiol would be expected to estradiol unless any unexpected results are seen.

Claims 27, 30, 32 and 33 are drawn to the doses of the estrogen compound. The determination to employ the optimum ranges of the estrogen compound would have been within the skills of the one familiar with the art.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill might reasonably infer from the teachings. *In re opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA 1976). A reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982).

Accordingly, the burden of proof is upon applicants to show that instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

2. Claims 22-34 are rejected under 35 U.S.C. 103(a) as obvious over Lanquetin et al. (US Patent 5,891,867). Lanquetin et al. teaches the method of treating estrogen deficiencies in menopausal women by the oral administration of an estrogen alone followed by the combination of estrogen progestogen combination and then a placebo. See the entire document especially lines 20-

62, col. 1, lines 16-67, col. 2, cols 3 and 4, lines 10-64, col. 5. These combination are useful for correction of estrogen deficiencies during natural or artificial menopause.

The instant claims differ from the reference in having different generic scope. The instant invention is broader than the prior art by claiming the simultaneous administration of estrogenic and progestative compounds for estrogenic deficiencies. The 17b-estradiol units for 10 days (D1 to day D10 days). The units of combination of 17b-estradiol and nomegesterol acetate for fourteen consecutive days (day D11 to day D25). The placebo units for six days (day D25 to day D30). See lines 25-62, col. 1). The amount of the active principle ranging from 1-3 mg of b estradiol, combination of estradiol and nomegestrol acetate ranging from 1-3 mg and 1.5 to 6 mg. The delay in the occurrence of bleeding after the treatment was stopped. See lines 28-59, col. 2.

One having ordinary skill in the art would have been motivated to prepare additional beneficial composition and method for the treatment of estrogenic deficiencies during menopause. the combination with a estrogen and a compound with progestational activity because prior art teaches that estradiol in combination with a progestative compound for the treatment of

estrogenic deficiencies. The treatment by the same combination for extended days would have been obvious to one who is familiar with the art. Note, that the total days of treatment by the prior art is 24 days, 14 consecutive using combination and 10 using estradiol alone.

There has been ample motivation provided by the prior art to prepare such combination when searching for the compositions of the similar activity.

Claim 26 is drawn to estradiol valerate are known esters and property associated with the estradiol would be expected to estradiol unless any unexpected results are seen.

Claims 27, 30, 32 and 33 are drawn to the doses of the estrogen compound. The determination to employ the optimum ranges of the estrogen compound would have been within the skills of the one familiar with the art.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill might reasonably infer from the teachings. *In re opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA 1976).

A reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982).

Accordingly, the burden of proof is upon applicants to show that instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

A typing error was found in line 5 of claim 34. The word "protestogenic" should be replaced by "progestogenic". Appropriate correction is required.

Telephonic Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha N. Qazi, whose telephone number is (703) 305-3910. The examiner can normally be reached on Monday through Friday from 8 a.m. to 6 p.m. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Sabiha N. Qazi Ph.D.

5/30/00

Examiner, Art Unit 1616